CLEAN VERSION OF AMENDMENTS

In the claims:

1. (Amended) A process for producing a stabilized cell for use as an internal control in methods for isolating and identifying rare cells, said stabilized control cell having determinants in common with said rare cells, said process comprising:

a) redundantly labeling said control cell with at least two fluorescent labels having the same spectral properties;

b) permeabilizing said control cell;

c) contacting said labeled cells with a cell fixative said fixative effecting stabilization of both cellular structure and antigenic moieties present on said control cells;

d) subsequently removing the excess fixative to promote long-term storage of said control cells, said control cells being physically and biologically stable for at least six months.

7. (Amended) A process for producing a stabilized cell for use as an internal control in methods for isolating and identifying rare cells, said stabilized control cell having determinants in common with said rare cells, said process comprising:

a) redundantly membrane labeling said control cell with at least two fluorescent labels having the same spectral properties;

b) contacting said labeled cells with a cell fixative said fixative effecting stabilization of both cellular structure and antigenic moieties present on said control cells;

c) subsequently removing the excess fixative to promote long-term storage of said control cells, said control cells being physically and biologically stable for [a period up to] at least six months, wherein said control cell expresses epithelial cell adhesion molecule (EpCam) on its surface and also expresses cytokeratin intracellularly.

9. (Amended) The process as claimed in claim 7, wherein said membrane labeling is selected from the group consisting of long chain lipophilic carbocyanines, long chain lipophilic indocarbocyanines, long chain lipophilic indodicarbocyanines, and analogs thereof, lipophilic aminostyryl dyes, and long chain analogs of C18 rhodamine B and C18 fluorescein dyes.

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10. (Amended) A stabilized cell, previously permeabilized, for use as an internal control in methods for isolating and identifying rare cells, said control cell having determinants in common with said rare cells, wherein said control cell is labeled redundantly with at least two fluorescent labels having the same spectral properties, and cellular components and antigenic moieties of said control cell have been stabilized for at least six months by exposure to fixative.

16. (Amended) A stabilized cell, previously permeabilized, for use as an internal control in methods for isolating and identifying rare cells, said stabilized control cell having determinants in common with said rare cells, and comprising a detectably labeled membrane, said cells further comprising stabilized cellular components and antigenic moieties, said stabilization being effected by exposure to a fixative, wherein said control cell is a tumor cell expressing EpCam on its surface and cytokeratin intracellularly.

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22. (Amended) The control cell as claimed in claim 16,said cell being an MCF-7 breast cancer cell, further comprising a second detectably labeled surface determinant which is an estrogen determinant.

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23. (Amended) The control cell as claimed in claim 16, said cell being an LNCaP prostate cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of PSMA, PSA, and androgen determinant.

24. (Cancel)

25. (Cancel)

26. (Cancel)

28. (Amended) A stabilized cell, previously permeabilized, for use as an internal control in methods for isolating and identifying rare cells, said stabilized control cell having determinants in common with said rare cells, and comprising a redundantly labeled membrane, said membrane being labeled with at least two fluorescent labels having the same spectral properties, said cells further comprising stabilized cellular components and antigenic moieties, said stabilization being effected by exposure to a fixative, wherein said control cell is selected from the group consisting of tumor cells, bacterially infected cells, virally infected cells, myocardial cells, and endothelial cells in circulation, and fetal cells in maternal circulation.

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35. (Amended) An improved method for detecting and enumerating rare cells in a mixed cell population, the presence of said rare cells in said population being indicative of severity of a disease state, comprising:

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a) obtaining a blood sample from a test subject, said sample comprising a mixed cell population suspected of containing said rare cells;

b) preparing an immunomagnetic sample wherein said blood sample is mixed with magnetic particles coupled to a ligand which reacts specifically with a determinant of the rare cells, to the substantial exclusion of other sample components;

c) contacting said immunomagnetic sample with at least one reagent which labels a determinant of said rare cells; and

d) analyzing said labeled rare cells to determine the presence and number of any rare cells in said immunomagnetic sample, the greater the number of rare cells present in said sample, the greater the severity of said disease state, wherein the improvement comprises the addition of a stabilized cell, previously permeabilized, for use as an internal control cell in said method, said control cell having determinants in common with said rare cells and wherein said membrane of said control cell is detectably labeled and cellular components and antigenic

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moieties of said control cell have been stabilized for [a period up to] at least six months by exposure to fixative.

41. (Amended) The method as claimed in claim 38, wherein the control cell is MCF-7 breast cancer cell, further comprising a second detectably labeled surface determinant which is an estrogen determinant.

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42. (Amended) The method as claimed in claim 38, wherein the control cell is an LNCaP prostate cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of PSMA, PSA, and androgen determinant.

43. (Cancel)

44. (Cancel)

45. (Cancel)

47. (Amended) An improved kit for screening a patient sample for the presence of circulating tumor cells, comprising:

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a) coated magnetic nanoparticles comprising a magnetic core material, a protein based coating material, and anti-EpCAM coupled, directly or indirectly, to said base coating material;
b) at least one antibody having binding specificity for a cancer cell determinant;
c) cell specific dye for excluding sample components other than said tumor cells from analysis wherein the improvement comprises the addition of a container comprising stabilized cells, previously permeabilized, for use as an internal control, said stabilzed control cells having determinants in common with said tumor cells, wherein said membrane of said control cell is detectably labeled, and cellular components and antigenic moieties of said control cells have been

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stabilized for at least six months by exposure to fixative, said stabilized control cells being suspended in a buoyant density medium.

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50. (Amended) The kit as claimed in claim 47, wherein the control cell is an LNCaP prostate cancer cell, further comprising a second detectably labeled surface determinant selected from the group consisting of PSMA, PSA, and androgen determinant.

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54. (Amended) The kit as claimed in claim 47, wherein the control cell is a C32 melanoma cancer cell, further comprising a second detectably labeled surface determinant which is a CD146 molecule.

Respectfully submitted,

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